

Methods: We evaluated the outcome for patients who presented in Killip II and III in the GUSTO IIb substudy, the largest randomized trial of direct PTCA versus thrombolysis.

Results: This CHF group was older (66.6 yrs vs 62.0 yrs, $p < 0.001$) and with higher rates of prior angina (51.6% vs 38.6%, $p = 0.016$), prior CHF (5.3% vs 1.3%, $p < 0.01$), and COPD (8.6% vs 1.7%, $p = 0.001$) than the Killip I group.

Conclusion: Although this is the largest number of patients with CHF randomized to PTCA vs thrombolysis, the sample size is small. These findings, while not statistically significant, raise the potential of a greater benefit for PTCA at 30 days and 6 months in patients presenting in Killip classes II and III complicating an AMI. A larger trial would be needed to resolve this issue, and to investigate a potential role for adjunctive therapy.

3:00

856-5 Benefit of Primary Angioplasty in Patients Presenting Late With ST Segment Elevation and Acute Myocardial Infarction

W.J. French, M.J. Sada. *For the National Registry of Myocardial Infarction (NRM-2) Investigators: Harbor-UCLA Medical Center, Torrance, California, USA*

Primary PTCA (1° PTCA) is used in treatment of patients with acute myocardial infarction, but its effectiveness in late presenters has not been defined. 3,550 pts were evaluated with ST elevation who presented more than 12 hrs after onset, but otherwise were eligible for thrombolytic therapy (TTx), and were enrolled in NRM-2 between 1994 and 1996. Pts in shock or who received TTx were excluded. The invasive group included 568 pts who underwent cath within 6 hrs of admission with 80% having 1° PTCA. The medical therapy (MTX) group included 84%, or 2,982 pts. The invasive group were younger (60.9 vs 65.7 yrs), more likely male (66.2 vs 59.6%) with a history of PTCA (8.1 vs 4.3%), but less likely to have had CHF (3.7 vs 8.1%) or CABG (4.6 vs 8.0%, all $p < 0.001$). Although pts in the invasive group were more likely to be in Killip class I (82.8 vs 77.7%, $p < 0.001$), other presenting characteristics were similar to pts in the MTX group. The invasive group were more likely to receive heparin (93.3 vs 81.5%), aspirin (89.8 vs 82.2%), and IV beta blockers (19.1 vs 14.2%, all $p < 0.001$) within 24 hrs of admission. In-hospital mortality in the invasive group was 2.8%, compared with 7.8% in the MTX group ($p < 0.001$). After multivariate adjustment, the invasive group were less likely to die than those in the MTX group (odds ratio 0.47, 95% confidence interval 0.27 to 0.82).

Conclusion: Pts with acute myocardial infarction who presented more than 12 hours after symptom onset appear to benefit from primary angioplasty.

3:15

856-6 Improving Outcomes in Patients Undergoing Primary Angioplasty for Acute Myocardial Infarction: Trend Data From the National Registry of Myocardial Infarction 2

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Although there is increasing use of angioplasty (PTCA) for acute myocardial infarction (MI), little data about trends are available. National Registry of Myocardial Infarction 2, an ongoing study, collects data that can be used to assess trends for this reperfusion modality. Data from five 6 month periods from July 1994 through December 1996 were analyzed.

Of over 100,000 patients with ST elevation receiving reperfusion, use of primary PTCA increased from 9.6% to 12.3%. There were no differences in mean age or proportion over 75 yrs, male, anterior MI, or with shock. All trends in the table are statistically significant. Mean door to balloon time and in-hospital mortality have decreased, although more patients are TIMI "not low risk." The use of stents and/or antiplatelet therapy other than aspirin has increased, while repeat PTCA has decreased.

Study Period	1	2	3	4	5
Primary PTCA (%)	9.6	9.9	11.4	12.0	12.3
Mean Door to Balloon (min)	179	164	160	159	157
TIMI not low risk (%)	44.1	44.8	47.5	47.1	49.9
Mortality (%)	7.4	7.5	6.8	6.3	
Non ASA Antiplatelet (%)	3.6	4.2	7.2	16.2	25.7
Stent (%)	6.6	8.6	12.4	20.9	24.8
Second PTCA (%)	17.9	14.1	12.2	12.7	10.7

These unadjusted trend data indicate increased use of primary PTCA, earlier therapy, and improving clinical outcomes.

857 Randomized Trials of Antihypertensive Agents

Tuesday, March 31, 1998, 2:00 p.m.-3:30 p.m.
Georgia World Congress Center, Room 365W

2:00

857-1 Blood Pressure Lowering in Patients With Cerebrovascular Disease: Results of the Randomized Post-stroke Antihypertensive Treatment Study (PATS)

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Background: The randomized Post-stroke Antihypertensive Treatment Study (PATS) aimed at determining whether antihypertensive drug treatment could reduce the risk of stroke incidence and other cardiovascular complications in patients with a history of stroke or transient ischemic attack (TIA).

Methods: A total of 5665 patients were randomized (2841 to active treatment, took 2.5 mg indapamide per day; 2824 to placebo took one tablet of placebo). Age (\pm SD) averaged 60 ± 8 years, 26% were women, and 64% were ischemic. Mean BP was 154/93 mmHg. In 913 (16%) subjects BP was below 140/90 mmHg.

Results: Average follow-up approximated to 2 years. The three-year average BP was 149/89 mmHg for the placebo group and 144/87 mmHg for the indapamide group, respectively. The three-year fatal and nonfatal stroke incidence rate was 12.1% for placebo and 8.2% for indapamide. The relative risk by proportional hazards regression analysis was 0.69 (95% CI: 0.57-0.85, $P < 0.001$). In 913 normotensive subjects the three-year cumulative stroke incidence rate was 8.7% for indapamide group and 4.9% for placebo group. Relative risk for all cause mortality was 0.92 (95% CI: 0.74-1.14, $P = 0.45$) in all subjects.

Conclusion: In post-stroke patients with or without high blood pressure, BP reduction of 5/2 mmHg with 2.5 mg indapamide per day reduced the fatal and nonfatal stroke incidence by 31%.

2:15

857-2 Effect of Ramipril After Acute Myocardial Infarction in Patients With Arterial Hypertension

C.S. Spargias, A.S. Hall, S.G. Ball. *Institute for Cardiovascular Research, University of Leeds, UK*

Background: After myocardial infarction (MI), patients with a history of arterial hypertension (AH) have a worse prognosis than that of normotensives. Angiotensin converting enzyme (ACE) inhibition post MI substantially improves survival in high risk populations. This study evaluates the influence of a history of AH on the efficacy of ACE inhibition post MI.

Methods: We retrospectively analyzed data from the AIRE study (randomized, placebo-controlled trial of ramipril in 2006 post MI patients with clinical evidence of heart failure-HF). At baseline, 28% of the patients had a history of AH. We examined the effect of ramipril on clinical outcomes according to whether or not a history of AH was present. To adjust for baseline clinical differences, 16 variables were simultaneously entered in a multivariate Cox regression model.

Results: Treatment with ramipril resulted in a significant reduction in the risk of all-cause mortality in the hypertensive patients (32%, CI 1% to 54%, $p = 0.04$) but not in the normotensive group (14%, CI -11 to 34%, NS). There was also an associated trend toward lower HF-morbidity in the hypertensives (31%, CI -4 to 46%, $p = 0.07$) but not in the normotensives (5%, CI -26 to 28%, NS).

Conclusion: Our data indicate that ACE inhibition, in patients with clinical evidence of HF post MI, is of particular benefit to those with a history of AH.

2:30

857-3 A "Paper-less" Study on Optimal Treatment Strategies for Hypertension and CAD: Pilot Phase Data From the International Verapamil-trandolapril Study (INVEST)

C.J. Pepine, M. Conlon, E. Handberg-Thurmond, R.G. Marks, R. Cooper-DeHoff, H. Robert Kolb. *University of Florida, Gainesville, Florida, USA*

The INVEST is a trial to assess whether a calcium antagonist treatment strategy is equivalent to a noncalcium antagonist strategy (JNC V) to prevent adverse outcomes in 27,000 patients with hypertension and CAD. Patients are being enrolled at 1,500 primary care sites using a novel electronic system for direct on-screen data entry, randomization and drug distribution from

a central mail-pharmacy all linked via the INTERNET. The INVEST system uses Netscape Enterprise web server and the Oracle Relational Database to collect and store eligibility, treatment, follow-up and management data. A SUN Microsystems Ultrasparc running Solaris 2.5 provides web services and acts as a firewall equipped with 2 Ethernet adapters for a private network running on Windows NT. A RAID system assures no loss of service for drive failure. The entire system is backed up by FAX/phone. All study-related information is stored in the system, has high level, artificial intelligence to assure protocol correct data entry and permit physicians to customize drug combinations and dosing schedules, within the randomly-assigned treatment strategies. Pilot phase data on 150 patients from 15 sites will be presented. This approach we believe, is the forerunner of on-line clinical trials for the next century.

2:45

857-4 Rate and Extent of Left Ventricular Hypertrophy Regression: A Comparison of Angiotensin II Blockade With Irbesartan and Beta-Blockade

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Background: The effects of antihypertensive therapy with the AT₁ receptor antagonist irbesartan (IRBE) on the regression of left ventricular hypertrophy (LVH) were compared to those of atenolol (ATEN) in a double-blind, 48-week study.

Methods: 115 hypertensive men and women with left ventricular mass index (LVMI, by echocardiogram) >131 g/m² and >100 g/m², respectively, were randomized to receive IRBE 150 mg or ATEN 50 mg qd. For seated diastolic BP (SeDBP) >90 mm Hg, doses were doubled at 6 weeks, supplemental HCTZ or fexofenadine was added in 6-week intervals thereafter as needed. LVMI, SeDBP, and neurohormones were measured at Weeks 12, 24, and 48.

Results: 48 IRBE and 53 ATEN patients completed the study. Baseline demographics were similar, mean BP, 162/103.6 mm Hg, LVMI (g/m²) men, 151; women, 128. Mean \pm SE changes from baseline were

Wk	IRBE		ATEN	
	LVMI (95% CI)	SeDBP	LVMI (95% CI)	SeDBP
12	5.76 \pm 3.59 (-12.9, 15)	9.2 \pm 1.5	0.45 \pm 2.95 (-6.4, 5.5)	12.0 \pm 1.0
24	9.12 \pm 3.72 (-1.66, 16)	12.2 \pm 1.2	4.51 \pm 2.94 (-10.4, 14)	14.3 \pm 1.1
48	19.66 \pm 4.07 (-27.9, 11.5)	18.0 \pm 1.4	11.97 \pm 2.93 (-17.9, 6.1)	16.6 \pm 1.1

By 48 weeks, 34% of IRBE and 45% of ATEN patients remained on monotherapy. Renin decreased with ATEN; renin and Ang II increased with IRBE consistent with AT₁ blockade. 67% of ATEN and 34% of IRBE patients reported adverse drug experiences.

Conclusions: Despite similar BP reductions with both regimens, LVH regressed sooner and to a greater degree with IRBE compared with ATEN. IRBE produced superior tolerability and end organ protection. The results support a role for Ang II in the development of LVH.

3:00

857-5 Effects of Single Drug Antihypertensive Therapy on Left Atrial Enlargement in Hypertension

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Background: Left atrial (LA) enlargement (E) is common in hypertension. We previously reported \downarrow in LA size on echo at 1 yr only with hydrochlorothiazide (HCTZ) despite efficacy of HCTZ, captopril (CAPT), and atenolol (ATEN) for BP and LV mass reduction. However the influence of LAE as well as age, race, and body weight (covariates known to influence LA size) on efficacy of drugs for reduction of LA size is unknown.

Methods: We used 2D-targeted M-mode echo to measure LA size in 587 men (av BP 152 \pm 14/99 \pm 3 mmHg, av age 59 \pm 10 yrs, 40% LAE) in a 15 center randomized double-blind trial of six active drugs: HCTZ, CAPT, ATEN, clonidine (CLON), diltiazem (DILT) and prazosin (PRAZ). Drug effects were statistically adjusted for age, race, body weight, and baseline LA size.

Results: While no changes occurred at 8 wks, at 1 yr pts with LAE had \downarrow in LA size [all p < .05, adjusted means (mm) \pm S.D.] with HCTZ (-3.2 \pm 1.1), ATEN (-4.2 \pm 1.1), CAPT (-3.2 \pm 1.1), CLON (-2.9 \pm 1.0) and DILT (-2.9 \pm 1.1) but not PRAZ (-0.3 \pm 1.1, pNS). Pts with normal baseline LA size had a \downarrow in LA size (p < .05) with CAPT (+2.7 \pm 1.0) and CLON (+3.8 \pm 1.0), with a trend for \downarrow with HCTZ (-1.6 \pm 1.0; 95% CL -3.5 to +0.3).

Conclusion: \downarrow in LA size with antihypertension therapy requires prolonged treatment. The magnitude of \downarrow differs between classes of agents and is affected by prior LAE, but not by interdrug differences in BP control or in reduction of LV mass.

857-6 Diuretics Preserve the Circadian Blood Pressure Profile in Hypertensive Patients

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Background: Normally blood pressure (BP) decreases during the night in normotensives and most hypertensives. The loss of nocturnal BP fall is known to be associated with an impaired prognosis. Little is known about the relative ability of different antihypertensive classes in preserving the diurnal pattern of BP. Thus we evaluated the circadian BP profile in a large cohort of hypertensive patients.

Methods: We enrolled 1502 consecutive subjects (aged 17-88 years; 50.9% males), who had been referred for assessment of hypertension. All patients performed a 24-hour ambulatory BP monitoring. A subset with stable therapy was identified (n = 704) and divided into five groups according to the drug treatment regime: ACE-inhibitors, β -blockers, calcium channel blockers, thiazides, or combined antihypertensive regimens.

Results: Patients on diuretics had significantly lower systolic BP during night-time compared to patients treated with ACE-inhibitors (p < 0.003), β -blockers (p < 0.02), and antihypertensive drug combination (p < 0.0001), but not versus calcium channel blockers (p = 0.1). Patients on diuretics presented a greater nocturnal diastolic BP fall compared to patients treated with ACE-inhibitors (p < 0.003), or antihypertensive drug combination (p < 0.02), but not versus patients with β -blockers (p = 0.1) or calcium channel blockers (p = 0.1).

Conclusion: Preservation of nocturnal BP fall using diuretics may contribute to the known reduction of cardiovascular morbidity and mortality in this class of drug. Utilization of diuretics as first-line antihypertensive therapy could result in a better cost-benefit ratio.

858 Metabolic Stress on Infection and Vascular Function

Tuesday, March 31, 1998, 2:00 p.m.-3:30 p.m.
Georgia World Congress Center, Room 257W

2:00

858-1 Infection With Chlamydia Pneumoniae Accelerates the Development of Atherosclerosis and Treatment With Azithromycin Prevents it in a Rabbit Model

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Chlamydia pneumoniae infection is associated with atherosclerosis by serologic studies and detection of bacterial antigen within plaque. We sought to evaluate a possible etiologic role in an animal model.

Thirty New Zealand white rabbits were given 3 separate intranasal inoculations of either *C. pneumoniae* (N = 20) or saline (N = 10) at 3 week intervals and fed chow enriched with a small (0.25%) amount of cholesterol. Infected and control rabbits were then randomized and begun on a 7 week course of azithromycin or no therapy. After three months, the rabbits were euthanized and sections of thoracic aortas blindly evaluated microscopically for maximal intimal thickness (MIT), percentage of luminal circumference involved (PLCI), and plaque area index (PAI) of atherosclerosis. MIT was increased in infected rabbits compared with uninfected controls: 0.55 (SE 0.14) mm vs 0.16 (SE 0.06) mm, p = 0.022, whereas MIT for infected rabbits receiving antibiotics was similar to uninfected controls (0.20 [SE 0.03]) and less than that of infected, untreated rabbits (p = 0.021). PLCI and PAI also increased after untreated but not treated infection. Immunofluorescent chlamydial antigen was detected in 2/9 untreated, 3/10 treated, and 0/10 control animals.

Conclusion: Intranasal *C. pneumoniae* infection accelerates intimal thickening in rabbits given a modestly cholesterol-enhanced diet and treatment with azithromycin after infectious exposure prevents it. These findings strengthen the etiologic link between *C. pneumoniae* and atherosclerosis and should stimulate further studies.